

RESEARCH PROTECTIONS UPDATE

News and Comment on the Protection of Human Subjects and Animals in Navy Research

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Comment

“Community Consultation” and Informed Consent

The Navy Human Research Protection Program (DON HRPP) staff considers informed consent to be a guiding principle for the protection of human subjects in research. Navy HRPP policy, provided in SECNAVINST 3900.39D, awaiting signature by the Secretary of the Navy, states that “voluntary informed consent is fundamental to ethical research with humans. Informed consent ... is a process that includes a thorough discussion with prospective subjects and/or their legally authorized representatives and continues for at least the duration of the research.”

Today, the HRPP is addressing consent when subjects who might benefit from investigative treatments are incapacitated by medical emergencies and unable to give consent.

The FDA’s regulations for exception from informed consent for emergency research became effective November 1, 1996. Since then, IRBs and investigators have struggled with interpreting and complying with the regulations, especially the requirements for community consultation, public disclosure, and informed consent procedures that might be feasible.

In August, the FDA announced

the availability of a draft guidance document entitled “Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors: Exception from Informed Consent Requirements for Emergency Research” and requested comment on the guidance (<http://www.fda.gov/OHRMS/DOCKETS/98fr/06d-0331-gdl0001.pdf>).

In conjunction with the draft guidance, the FDA also will hold a public hearing on emergency research conducted without informed consent on October 11, 2006. The FDA wants to hear from individuals and groups who have encountered challenges in the conduct of emergency research in the absence of informed consent, including patient advocacy groups, individuals who have participated in clinical studies, Institutional Review Board members, sponsors, and other interested parties.

The topic is explored in an article by Charles Contant Ph.D., Laurence B. McCullough Ph.D., Lorna Mangus MPH, Claudia Robertson MD, Alex Valadka MD, and Baruch Brody Ph.D., in *Critical Care Medicine* (Vol.34, No.8). The authors note that new FDA regulations allow a waiver of informed consent “with additional protec-

tions, one of which is community consultation.”

The authors say that while “community consultation substitutes for individual consent” in an emergency setting, the regulations don’t define “consultation” or “community representative.”

They surveyed residents of Harris County, Tex., in conjunction with a study on the merits of a treatment for reduced cerebral blood flow after traumatic brain injury.

The researchers provided information on the treatment, risks and benefits, and sought responses to a series of statements, including: “If I or a close member of my family suffered a severe head injury, I would want to participate in the study.” The second part of that

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Clinical Trials Registration

Clinical Trials Registry On-Line at ClinicalTrials.gov

The International Committee of Medical Journal Editors (ICMJE) requires registration of clinical trials in a public trials registry prior to enrollment of the first subject, as a condition for publication in any of the ICMJE's 11 member journals. The policy applies to clinical trials starting enrollment after July 1, 2005, though there was a provision to register ongoing trials by September 13, 2005.

The ICMJE, in announcing the policy, said that "If all trials are registered in a public repository at their inception, every trial's existence is part of the public record and the many stakeholders in clinical research can explore the full range of clinical evidence."

The Committee continued that "For this purpose the ICMJE defines a clinical trial as any research project that prospectively assigns human subjects to intervention or comparison groups to study the cause-and-effect relationship between a medical intervention and a health outcome." Additionally, in an update of May 2005, the ICMJE provided that a "trial must have at least one prospectively assigned concurrent control or comparison group" to trigger ICMJE registration requirements. Trials are excluded from the ICMJE's registration requirement "if their primary goal is to assess major unknown toxicity or determine pharmacoki-

netics (phase 1 trials)."

Apart from the ICMJE policy, registration also may be required by law, for example, for investigational new drug (IND) efficacy trials for serious or life threatening diseases and conditions, conducted under FDA regulation.

The DON HRPP recommends that Navy researchers register their clinical trials on the public website, <http://www.ClinicalTrials.gov>, which is maintained by the National Library of Medicine of the National Institutes of Health (NIH).

NIH says that www.ClinicalTrials.gov is a directory of federally and privately supported clinical research conducted in the U.S. and around the world to test the effect of experimental drugs, devices, and procedures for many diseases and conditions. The website says that it accepts registration of all clinical trials approved by a human subject review board and that conform to the regulations of the appropriate national health authorities.

Trials are registered by means of a web-based data entry system called the Protocol Registration System or PRS. The website <http://prsinfo.ClinicalTrials.gov> provides extensive information on registration policies and procedures.

"Community Consultation" and Informed Consent

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statement then was amended as: "... I would not want to participate in the study."

While 79.75 percent said they would be willing to participate, only 67.78 percent thought that the benefits justified the risk, and only 57.66 percent thought the waiver of consent was justified. The authors found that "a substantial level of concern exists even when the risks of the investigation are [as] low [as in the current example.]"

The researchers add that community consultation can

be looked at as a means of obtaining community *input, approval, or consent*. They note that "The last approach is ethically questionable, when the subject is the individual patient, as opposed to the community as a whole."

"Investigators need greater guidance from regulators and IRBs about these crucial questions." They reiterate that "current regulations say nothing about what investigators should do with the results of community consultations," and note that even low-risk investigations face "unexpected community opposition."

New management at ONR 343

Singer Takes Helm of ONR's Research Protections Team

Dr. Tim Singer has been named director of the newly established Research Protections Division at the Office of Naval Research (ONR 343). Singer had been serving as acting head of 343; previously, he led ONR's Medical & Biological S&T division. ONR's Research Protections Division provides support and expertise to the DON HRPP for human research protection in the Navy's



Tim Singer

Systems Commands, operational and training commands, and extramural sites that conduct Navy-supported research.

"Our approach will be to do all we can to help commanding officers and extramural researchers protect human subjects in research, while recognizing that Fleet / Force

commands have critical operational missions to perform," he told **RPU**.

Singer, an aerospace experimental psychologist, retired from the Navy in 2002 after 32 years of military service—22 with the Navy. He served as an Army enlisted man prior to attending college.

A 1973 Phi Beta Kappa graduate of Reed College, he earned M.S., M. Phil., and Ph.D. degrees at Yale University.

In 1976, he received an Air Force commission and served as a USAF Biomedical Sciences officer before transferring to the Navy in 1980. He won his Navy wings in 1981.

His background includes extensive work on the impact of human factors on the development of aircraft systems. Early in his career he served as special sys-

tems manager for the Crew Systems division at the Naval Air Systems Command, where he directed the engineering development phase of NAVAIR's Advanced Technology Crew Station program.

In the late 1980s, he led a group of 110 scientists and engineers as superintendent for the Human Factors and Protective Systems division at the Naval Air Development Center.

In 1986, Singer was selected as a Navy NASA Mission Specialist Astronaut candidate. He has lectured at the Naval Academy and served as an adjunct assistant professor of health care sciences at the George Washington University School of Medicine.

Before coming to ONR, he commanded the 11 worldwide facilities and 1,250-member staff of the Naval Medical Research and Development Command in Bethesda, Md.

In January 2005, then-Chief of Naval Research Rear Adm. Jay Cohen directed him to stand up the DON HRPP Working Group. He became acting head of ONR 343 last year.



An E-2C patrol aircraft lands on the USS Theodore Roosevelt underway in the Atlantic. (USN photo)

DON Animal Research Protection Program

Successful Second-Level Administrative Review

By COL Mark Gold

Animal research protocols may seem to be more complex than brain surgery, but getting them past second-level administrative review is straight forward. In fact, it is simply a matter of following the direction provided in the protocol template of SECNAVINST 3900.38C (AR 40-33), "The Care and Use of Laboratory Animals in DOD Programs."

From an administrative perspective, most protocols have only a few issues requiring redress, and, if graded, easily would earn an "A." Many of those with more than one or two issues were prepared using outdated templates, templates without attached instructions, or by "cut and paste" from other protocol formats without referencing current requirements.

We offer our assistance to extramural or intramural facilities in modifying protocols to meet our unique standards."

The Office of Veterinary Affairs recognizes the local Institutional Animal Care and Use Committee's (IACUC's) authority to review, approve, and oversee intramural work as authorized by federal law. As such, our office will only conduct our second-level review after the local IACUC completely reviews and approves a protocol.

Many extramural IACUCs have little or no experience with the DOD template, and do their best in this foreign setting, applying their own intramural standards to the form, whereas intramural laboratories usually have more experience with the DOD standards. In the former case, our efforts focus on educating the PI and extramural IACUC about DOD standards, and in the later, on providing a quality assurance tool. None-

theless, we offer our assistance to extramural or intramural facilities in modifying protocols to meet our unique standards and complete the second-level review process.

Some of the most frequently raised points:

Literature searches: Search the mandated databases, don't be afraid to find and discuss previous work, and state clearly if your work is duplicative or not.

Data analysis: Select your statistical tests and values, and justify your group sizes before beginning work.

Animal numbers: Scientifically justify all animals to be used. Do not justify animal use by some arbitrary time frame; be consistent throughout the protocol

Assurances: The PI must circle pain relief intent and sign the document.

Technical procedures: Reference procedures or explain in detail so that the IACUC can evaluate or another scientist can repeat the work.

Endpoints: List all expected and alternative endpoints (e.g., address when animal use will be completed or, alternatively, when animals may be removed from the study.)

We respect the great number of issues that every PI must address in completing the DOD protocol template, and know that sometimes one or two slip through the cracks.

The Office of Veterinary Affairs is available to assist. Don't hesitate to contact me at 202-762-0253, or SSG James at 202-762-0252.

Col. Mark Gold, USA, is Director of Veterinary Affairs in the Office of Research Protections at the Bureau of Medicine and Surgery.

**In association with the
2006 PRIM&R - ARENA
HRPP Conference,
Washington, DC,
November 14, 2006**

**Human Research
Protection Programs:
DoD-Unique Perspectives**



HRPP Visits Navy Safety Center

ONR HRPP Leaders Explore Safety Center Programs

Dr. Tim Singer, director of the Research Protections Division at the Office of Naval Research and deputy director Lt. Cdr. William Deniston visited the Navy Safety Center (NSC) in Norfolk, Va., in late August for discussions with NSC officials on the Center's management initiatives for Navy safety programs, and to evaluate NSC's data management system.

Singer says that the NSC's initiatives to enhance safety are "based on a unique philosophy of operational risk management that considers safety a critically important component of operational success."

The ONR Research Protection Division stood up last year as a component of the Navy Human Research Protection Program (DON HRPP) to provide support and expertise for human research protections in Fleet / Force operational commands, the Navy's Systems Commands, training commands, and Navy-supported extramural research. Singer, a retired Navy captain with extensive research and operational experience in naval aviation, was named director of the division last month. (see page 3).

that the Research Protection Division will work to support Fleet / Force operators' missions, while enforcing human research policies.

The Navy Safety Center monitors safety programs for the surface, undersea, and aviation communities, as well as motor vehicle safety for sailors and Marines. The Center's data-management system, called the Web-Enabled Safety System (WESS), provides capabilities that the DON HRPP potentially could adapt to monitor information on Navy human subject research, including active and completed protocols, personnel training status, and Institutional Review Board decisions.

The DON HRPP is surveying information-management systems used by several Navy commands, non-defense federal agencies, and universities to monitor human subject research data, in order to develop a design plan for a DON HRPP system.

Singer says that the WESS "offers much of value" for human research protection. The DON HRPP staff is looking at benchmarking features of the NSC system.

He adds that the HRPP team also is interested in the Safety Center's method for getting its message out to commanders deployed and at home, on reducing motor vehicle accidents, which today are a major cause of fatalities among military personnel.

Singer says that "Like the DON HRPP, the Safety Center must address a wide range of settings to carry out its mission to track information on mishaps, conduct inspections, and provide accountability to Navy leadership about the care of Navy personnel and resources."

He points out that a key requirement of an effective program, both for DON HRPP and for the Safety Center, is development of metrics that measure success. Such metrics, he says, answer the question "How do you know whether what you're doing works?"

The DON HRPP staff is working to schedule additional visits to Navy facilities to learn more about tracking key personnel safety data, as well as to monitor compliance with Navy and federal policy on protection of human subjects in research.



The amphibious assault ship USS Iwo Jima (LHD 7) conducts flight operations in the Arabian Sea. (USN photo)

He says that the Safety Center's program shares many elements in common with the DON HRPP, particularly an approach to "optimizing safety of personnel and equipment for Navy missions." He stresses

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**Marriott Wardman Park Hotel
2660 Woodley Road, NW
Washington, DC 20008
November 14, 2006 - 0800-1630**

- 0800-0815 **Welcome and Introductions**, Dr. Bob Foster, DDR&E
- 0815-0915 **Then and Now – The Evolution of DoD HRPP**, Mr. Jay Winchester
A captivating briefing on the unique history of HRPP in DoD through the present day. Why DoD has specific requirements (e.g., 10 USC 980). How recent events such as the Gulf War have and how today's challenges (Iraq, PTSD, BioShield, etc.) impact our policies and programs.
- 0915-1045 **HRPP: Where You Stand Depends on Where You Sit**
A moderated panel will use a case study to present the various elements of a Human Research Protection Program.
- 1105-1205 **3 C's – Communication, Cooperation, & Collaboration**
A panel of the Army, Navy, and Air Force Surgeons General and Office of the Secretary of Defense for Personnel and Readiness will discuss the 3 C's.
- 1205-1330 Lunch with Mr. Young, DDR&E, as speaker
- 1330-1500 **DoD Component Breakout Sessions**
Army, Navy, Air Force, OUSD(P&R), and Joint Components (NSA, DARPA, DTRA, NGA, JFCOM, SOCOM & ASD(SO/LIC)) – will have component-specific sessions.
- 1520-1630 **Topic Breakout Sessions – Select a topic of interest**
Research in International Settings
Challenges in Defining Research with Human Subjects
Social-Behavioral Research
"Rules of Engagement"
- Adjourn

On-line registration will begin soon via the DD&RE website

No registration fee for the one-day HRPP: DoD-Unique Perspectives session

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